

NONPROVISIONAL APPLICATION FOR LETTERS PATENT

UNITED STATES OF AMERICA

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in

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**NONFLAMMABLE ETHYLENE OXIDE GAS BLEND COMPOSITIONS, METHOD OF
MAKING SAME, AND METHOD OF STERILIZATION**

of which the following is a specification:

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TECHNICAL FIELD

The present invention relates generally to a method for sterilization, fumigation, and disinfection, and more particularly to gas compositions comprising ethylene oxide,
20 carbon dioxide, and trifluoromethyl iodide, and methods of making and utilizing such compositions.

BACKGROUND OF THE INVENTION

The three primary methods utilized for sterilization are autoclaving (exposure to high pressure, high temperature steam), irradiation with gamma or beta rays, and exposure to ethylene oxide (EtO). Sterilization via exposure to EtO is utilized for items that might be harmed by the other methods, or when EtO sterilization presents a more convenient and cost-effective alternative. EtO is highly effective in rendering microorganisms nonviable. However, EtO has a flash point below -20°F and is explosive over a wide range of concentrations in air, generally from 3% to 100%. Additionally, because EtO contains its own oxidizer, it is explosive, with or without the presence of oxygen in air.

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By adding one or more gaseous flammability suppressants to EtO, it is possible to produce nonflammable gas blends useful as sterilants, fumigants, and disinfectants. Heretofore, dichlorodifluoromethane (CF_2Cl_2 ; also called chlorofluorocarbon-12 or CFC-12) has been used to render EtO inert, and nonflammable in a blend consisting of 88% CFC-12 and 12% EtO by weight. This mixture comprises about 27% EtO by gas volume. However, CFC-12 has been implicated in

stratospheric ozone depletion, and thus its production has been banned under the provisions of the Montreal Protocol. Interim replacements for CFC-12 in sterilant gas blends have been developed. One widely-used mixture consists of EtO with

5 chlorodifluoromethane (CHF_2Cl ; also called hydrochlorofluorocarbon-22 or HCFC-22) and $\text{C}_2\text{H}_2\text{F}_4\text{Cl}$ chlorotetrafluoroethane (HCFC-124). The nonflammable blend of EtO with HCFCs 22 and 124 contains 10% by weight EtO, corresponding to about 23% by gas volume. This blend is

10 disadvantageous in that it must be used at slightly higher pressure than the 88:12 blend of CFC-12:EtO to obtain the same effectiveness. Although HCFCs have a much lower ozone-depletion potential (ODP) than CFCs, HCFCs are still considered problematic and their production will be phased out

15 under the terms of the Montreal Protocol and its associated amendments. For example, HCFC-22 production in the U.S decreased by 30% in 2003.

In many applications the trend has been to replace HCFCs

20 with hydrofluorocarbons (HFCs). HFCs do not deplete stratospheric ozone, are generally low in toxicity, and are compatible with most materials. HFCs with high fluorine content are flammability suppressants. Disadvantageously,

however, HFCs cost more to produce than CFCs or HCFCs, and contribute to global warming. Unfortunately, replacing HCFC inerting agents with HFC inerting agents in nonflammable EtO gas blends will increase the cost of the blends, and will
5 cause the blends to have higher global warming potentials (GWPs). **Table I** lists flammability suppressants utilized in EtO blends, and their estimated atmospheric lifetimes and GWPs.

10

Table I

**Atmospheric Lifetimes and GWPs of Fluorinated Flammability
Suppressants utilized in EtO Blends.**

Chemical Name	Designation	Atmospheric Life (yrs)	GWP relative to CO ₂ , 100-yr
dichlorodifluoromethane	CFC-12	102	8100
chlorodifluoromethane	HCFC-22	12	1500
chlorotetrafluoroethane	HCFC-124	6	470
pentafluoroethane	HFC-125	33	3800
2H-heptafluoropropane	HFC-227ea	36	3800

Sterilizations via exposure to EtO are commonly performed
15 at temperatures near 50°C with EtO concentrations of 500 to 700 mg/L. At these concentrations, sterilization cycles can last hours depending on the materials being sterilized and the

configuration of same in the sterilization chamber. Palettes of boxed products in a large sterilization chamber require much longer sterilization time than individual items in a small sterilization chamber. Sterilization may also be
5 achieved at lower EtO concentrations for longer exposure times, although the Food and Drug Administration specifies 500 to 800 mg/L for sterilization of medical equipment. The Association for the Advancement of Medical Instrumentation recommends a minimum of 400 mg/L EtO.

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Some users have employed blends of carbon dioxide and EtO. When tested according to the ASTM E-681 test, "Concentration Limits of Flammability of Chemicals," the maximum concentration of EtO in carbon dioxide for
15 nonflammability is about 9%. A nonflammable blend of 8.5% EtO in carbon dioxide is available commercially. Although this blend is inexpensive and atmospherically friendly, it is particularly disadvantageous in requiring a high pressure of about 4 atm (59 psia) to provide 600 mg/L EtO at 54°C, and in
20 requiring specialized equipment to adequately contain the EtO in order to prevent exposure to personnel outside the sterilization chamber. Other compositions employ a blend of 20% EtO and 80% carbon dioxide (by moles), and, although less

flammable than pure EtO, is still flammable by the ASTM E-681 test. Such compositions require a pressure of about 2 atm (29 psia) to provide 600 mg/L EtO at 54°C and, as such disadvantageously require containment suitable to prevent
5 exposure to EtO by those performing the sterilization process.

In recent years the use of pure EtO for sterilization has become more prevalent, mainly because of its low cost and low pressure requirements. Pure EtO is less expensive per pound
10 of EtO than any nonflammable blend containing EtO, as there is no additional cost for the added blending agent(s). Moreover, because the pressure of pure EtO at 600 mg/L and 54°C is below one atmosphere, any leakage occurs inward instead of outward, therefore minimizing the potential of exposing personnel
15 thereto. Almost all contract sterilization companies now utilize pure EtO. Additionally, many smaller sterilization chambers are now made for use with pure EtO, and thus, are increasing in prevalence in medical facilities. However, use of pure EtO is disadvantageous in older EtO sterilizers, many
20 of which are still in service and not designed for use with pure EtO. Owners of such older equipment must make a large investment in new equipment and in training personnel to operate same and handle pure EtO. Because of the extremely

high flammability of EtO, such special equipment and safety precautions are required to minimize the flammability and exposure risks of utilizing same. Despite such precautions, however, at least ten accidents have occurred within the past
5 seven years at facilities utilizing pure EtO for sterilization, some resulting in serious injuries, and in at least one case, death.

As such, there remains a continuing need for nonflammable
10 blends containing ethylene oxide that are environmentally friendly and can deliver sufficient EtO for adequate sterilization, fumigation, and disinfecting at modest pressures and low cost, thereby reducing/avoiding operational and/or occupational hazards associated with use of available
15 EtO blends.

BRIEF SUMMARY OF THE INVENTION

Briefly described, in a preferred embodiment, the present
20 invention overcomes the above-mentioned disadvantages and meets the recognized need for such compositions by providing a nonflammable EtO gas blend for sterilization, fumigation, and disinfection.

The present invention preferably comprises a combination of carbon dioxide (a physically-acting combustion suppressant) and small amounts of trifluoromethyl iodide (a chemically-
5 acting combustion suppressant). The resulting combination acts as a synergistic combustion suppressant. The CO₂ and CF₃I combination is further preferably combined in a blend with EtO for use as a sterilant.

10 A feature and advantage of the present invention is its provision of highly synergistic flammability suppression by the combination of chemically-acting and physically-acting inertants.

15 A feature and advantage of the present invention is its provision of an EtO gas blend that sterilizes effectively at pressures below 25 psig.

A feature and advantage of the present invention is its
20 provision of a low-cost nonflammable EtO gas blend.

A further feature and advantage of the present invention is its suitability for utilization as a nonflammable EtO gas

blend compatible with most materials of construction of medical equipment and sterilization chambers.

A feature and advantage of the present invention is its
5 provision of a nonflammable EtO blend having components completely miscible in the liquid phase.

Another feature and advantage of the present invention is its provision of a nonflammable EtO gas blend that causes no
10 stratospheric ozone depletion.

An additional feature and advantage of the present invention is the provision of a nonflammable EtO gas blend that causes no significant global warming.
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Yet another feature and advantage of the present invention is its nonflammability.

These and other features and advantages of the present
20 invention will become more apparent to one skilled in the art from the following description and claims.

DETAILED DESCRIPTION OF THE PREFERRED AND SELECTED ALTERNATE
EMBODIMENTS

In describing the preferred and selected alternate
5 embodiments of the present invention, specific terminology is
employed for the sake of clarity. The invention, however, is
not intended to be limited to the specific terminology so
selected, and it is to be understood that each specific
element includes all technical equivalents that operate in a
10 similar manner to accomplish similar functions.

An attractive nonflammable EtO gas blend should possess
all of the following desirable properties: zero ozone-
depletion potential, complete miscibility of the components in
15 the liquid phase, low cost, effective operating pressures
below 40 psig, high effectiveness against a wide range of
microorganisms, nonflammability, highly synergistic
flammability suppression by the inerting components,
compatibility with most materials of construction of medical
20 equipment and sterilizer chambers, and extremely low global
warming potential.

Although it is relatively easy to find blends that satisfy some of the above-cited criteria, it is extremely difficult to identify blends that meet all such criteria. As such, the present invention meets a long-felt need in
5 providing chemical blends that meet all the above-cited criteria.

The key to achieving a highly effective nonflammable EtO blend is identifying miscible, highly effective combustion
10 suppressants for EtO, such that a high percentage of EtO can be utilized in the blend. Combustion suppression agents can be broadly classified as chemically-acting or physically-acting. Chemically-acting agents, such as, for exemplary purposes only, trifluoromethyl iodide, inhibit combustion
15 without the need for other agents by providing chemical species that remove flame propagating radicals from the combustion zone. In fact, the inventors of the present nonflammable EtO gas blend have found that trifluoromethyl iodide inhibits the combustion of EtO. Physically-acting
20 agents, such as, for exemplary purposes only, carbon dioxide, inhibit combustion without the need of other agents, by removing heat energy from the combustion zone, absorbing the energy in internal molecular motion. In fact, the present

inventors have further found that carbon dioxide inhibits the combustion of EtO. In some cases, when small amounts of chemically-acting combustion suppressants are added to physically-acting combustion suppressants, synergistic
5 combustion suppression has been observed by the present inventors. It has also been noted by Sheinson et al., but not with the present combinations. Synergistic combustion suppression is defined as the combination of two suppressants wherein the resulting combination is more effective than would
10 be expected by linear combination alone.

Through testing, the present inventors have found that trifluoromethyl iodide (CF_3I) attractively performs as a chemically-acting flammability suppressant having desirable
15 environmental properties. Trifluoromethyl iodide is one of the most effective stable gaseous chemically-acting combustion suppressants known. When released into the atmosphere, exposure to ultraviolet light rapidly photolyzes the carbon-to-iodine bond, causing the compound to decompose rapidly,
20 ultimately forming carbon dioxide, fluoride, and iodide, all naturally-occurring substances with minimal environmental impacts. Trifluoromethyl iodide has an atmospheric lifetime of less than two days and when released does not survive long

enough to reach the stratospheric ozone layer, and thus does not deplete stratospheric ozone. Trifluoromethyl iodide also has an extremely low GWP.

5 The present invention preferably comprises a combination of carbon dioxide (a physically-acting combustion suppressant) and small amounts of trifluoromethyl iodide (a chemically-acting combustion suppressant). The resulting combination acts as a synergistic combustion suppressant. The CO₂ and CF₃I
10 combination is further preferably combined in a blend with EtO for use as a sterilant. Preferably, the composition of the blends ranges from approximately 61 to approximately 88.5 percent by gas volume of CO₂, from approximately 11 to approximately 24 percent by gas volume of EtO, and from
15 approximately 0.5 to approximately 15 percent by gas volume of CF₃I. (Since all three gases are at the same temperature and pressure, the percentage by gas volume will equal the percentage by moles, and, as such, may be used interchangeably.) Preferably, the concentration of EtO is
20 maintained between 250 and 800 mg/L. Additionally, water vapor is preferably added to the above blends in an amount suitable to provide approximately 30 percent to approximately 70 percent relative humidity. Additives, such as, for

exemplary purposes only, trifluoromethane, pentafluoroethane, 1,1,1,2-tetrafluoroethane, 1,1,1,3,3-pentafluoropropane, 2H-heptafluoropropane, and/or other suitable hydrofluorocarbons, hydrofluoroethers, perfluorocarbons, nitrogen, argon, and air are also preferably included in the blend for serving as inert propellants when the blend is stored in a container for subsequent use. It should be recognized that the present combination of CO₂ and CF₃I provides unexpectedly high synergistic combustion suppression of EtO, heretofore unknown, and that could not have been predicted. Because carbon dioxide is inexpensive, and only a small amount of the more expensive trifluoromethyl iodide is needed, the overall nonflammable compositions are relatively inexpensive. The synergistic combustion suppression allows for higher concentrations of EtO than would otherwise be possible without expensive materials or containment, thus providing blends that are effective at reasonable pressures. Trifluoromethyl iodide is also an excellent solvent for many other chemicals and enhances mixing of EtO and carbon dioxide, which otherwise might have a tendency to separate. In liquid form, the three components of the blend, EtO, carbon dioxide and trifluoromethyl iodide, are miscible.

As noted above, carbon dioxide and trifluoromethyl iodide have much lower GWPs in comparison with the HCFC and HFC flammability suppressants utilized for inerting EtO. Carbon dioxide has an atmospheric lifetime of about 120 years and a 100-year GWP of 1 by definition. The amount of carbon dioxide released from implementation of sterilization operations utilizing the present EtO gas blend would be an extremely small fraction of global carbon dioxide release. In addition, the carbon dioxide used to make the blend would have been released anyway, so has no net effect on global warming. Trifluoromethyl iodide has an atmospheric lifetime of less than two days (less than 0.01 years) and an estimated 100-year GWP of 2. Therefore the blends described herein have much lower atmospheric impact than blends containing HCFCs or HFCs.

Testing by the present inventors, and by third party laboratories, has shown that trifluoromethyl iodide is thermally stable and compatible with most materials, including EtO and common metals and polymers found in sterilization equipment. Carbon dioxide has been well studied and shown to be compatible with most materials. The blends of EtO with carbon dioxide and trifluoromethyl iodide described herein satisfy all of the criteria listed above, thus satisfying a long felt need for an attractive nonflammable EtO gas blend.

Industrial Applicability:

This invention is further illustrated by the following non-limiting examples. The following hypothetical examples
5 show the effectiveness of the agents listed as low-cost, nonflammable, non-ozone-depleting, low-global warming EtO gas blends.

Example 1

10 In a hospital, clinic, dental office, or veterinary office, a variety of equipment that would not withstand autoclaving is placed into a small sterilization chamber rated to withstand 15 psig. The chamber is maintained at about 50°C, most of the air is evacuated (to less than two psia),
15 and a blend consisting of 74% carbon dioxide, 20% ethylene oxide, and 6% trifluoromethyl iodide by gas volume is introduced to a blend pressure of 26.6 psia. Water vapor is introduced, such as, for exemplary purposes only, by the introduction of steam, to maintain about 50% relative humidity
20 or about 1 psi water vapor, for a total system pressure of 28.6 to 29.6 psia or 13.9 to 14.9 psig. The exposure lasts for enough time to sterilize the equipment based on analysis of biological indicators, such as, for exemplary purposes

only, spore strips. After exposure, the chamber is evacuated and purged with filtered air to remove residual ethylene oxide. As a result of this procedure, the equipment is sterilized, as is the chamber, no flammability risk has been incurred, and the cost of the sterilant is significantly lower than other nonflammable sterilant gas blends usable in such equipment. Additionally, there is no contribution to ozone depletion or significant global warming.

10 Example 2

Palettes loaded with boxes of hemodialyzers in their packaging are preheated in moist air then placed into a sterilizer chamber rated to withstand 40 psig. Most of the air in the chamber is evacuated, leaving an air pressure of about one to two psi. The chamber is maintained at 54°C. Introduced into the chamber is a nonflammable blend consisting of 11% ethylene oxide, 88.5% carbon dioxide, and 0.5% trifluoromethyl iodide by gas volume. This blend is introduced up to a blend pressure of 48 psia (33 psig), giving a concentration of ethylene oxide of 600 mg/L. The relative humidity in the chamber is maintained at about 50%, giving about one psi of water, for a total pressure of 50-51 psia, or 35-36 psig. The exposure lasts for 12 hours, then the chamber

is evacuated through a scrubber that removes ethylene oxide before venting the remaining gases. The chamber is then purged with filtered air to remove residual ethylene oxide. As a result of this procedure, the hemodialyzers are
5 sterilized within their packages, no flammability risk has been incurred, the cost of the sterilant is significantly lower than other nonflammable sterilant gas blends with operating pressures less than 40 psig, and there has been no contribution to ozone depletion or significant global warming.

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Example 3

A government or industrial building is contaminated with a biological warfare agent such as anthrax spores or smallpox virus. Personnel are evacuated to medical facilities, and the
15 building cannot be reoccupied until it is decontaminated. The building is sealed and a nonflammable blend consisting of 61% carbon dioxide, 24% ethylene oxide, and 15% trifluoromethyl iodide by gas volume is introduced into the building, while air is allowed to escape through a scrubber or catalytic
20 oxidizer that destroys any escaping ethylene oxide. The gas is allowed to remain inside for a period of time estimated to be sufficient to render the biological agent nonviable (one to several days). Meanwhile the concentration of ethylene oxide

is monitored and more of the nonflammable gas blend is added as needed to maintain a level of approximately 300 to 400 mg/L ethylene oxide. At the end of the disinfecting time, fresh air is pumped in and the gas passes out through the scrubber or catalytic oxidizer. Air is then circulated through the building and a scrubber or catalytic oxidizer until monitoring shows levels of ethylene oxide below 1 ppm, the acceptable exposure level. Testing shows that no viable biological warfare agent remains, and the building is then unsealed and can be reoccupied. Through use of this procedure no flammability risk is incurred, no sensitive equipment is harmed, the biological warfare agent is destroyed, even in hidden areas, the building is returned to service quickly, no personnel are exposed to toxic disinfectants, and no ozone depletion or significant global warming resulted.

Example 4

At or near a postal or package facility, mail and packages are placed into a sterilization chamber rated to 25 psig. Most of the air is evacuated and into the chamber is introduced a blend of 86% carbon dioxide, 13% ethylene oxide, and 1% trifluoromethyl iodide by gas volume to a pressure of 33.9 psi, corresponding to 500 mg/L EtO. Including residual

air and 50% relative humidity, the total chamber pressure is 22.2 psig (36.9 psia). The mail and packages are exposed to the gas for a period of time sufficient to kill hazardous microorganisms, such as, for exemplary purposes only, two
5 hours. The gas is then evacuated from the chamber through a scrubber or catalytic oxidizer and the chamber is purged with air to remove residual EtO. As a result of this procedure the mail and packages are rendered free of pathogenic organisms.

10 Example 5

A load of spices is placed into a fumigation chamber and most of the air is evacuated. Into the chamber is introduced a blend of 88.5% carbon dioxide, 11% ethylene oxide, and 0.5% trifluoromethyl iodide by gas volume to a pressure of 40.1
15 psia, corresponding to 500 mg/L EtO. Including residual air and 50% relative humidity, the total chamber pressure is 28.4 psig (43.1 psia). Sufficient exposure time is allowed to kill undesirable organisms. The chamber is evacuated, then purged with air to remove residual EtO. As a result of this
20 procedure the spices are rendered free of plant and animal pathogens, without the risk of flammability.

Example 6

A passenger cruise liner has been the site of repeated outbreaks of a contagious bacterium or virus and must be decontaminated. After removing water and foodstuffs, opening
5 internal doorways and closing openings to the outside (e.g. closing external windows and sealing exterior doorways), a nonflammable blend consisting of 74% carbon dioxide, 20% ethylene oxide, and 6% trifluoromethyl iodide by gas volume is pumped into the ship, while air is allowed to escape through a
10 scrubber or catalytic oxidizer that destroys any escaping ethylene oxide. The ship is sealed and the gas is allowed to remain inside for one to several days. Meanwhile the concentration of ethylene oxide is monitored and more of the nonflammable gas blend is added as needed to maintain a level
15 of approximately 250 to 300 mg/L ethylene oxide. At the end of the disinfecting time, air is circulated through the ship and a scrubber or catalytic oxidizer until residual ethylene oxide concentration is below 1 ppm. The ship is then unsealed and can be safely returned to service. Through use of this
20 procedure no flammability risk was incurred, the pathogenic agents were destroyed, even in hidden areas, the ship was returned to service quickly, no personnel were exposed to

toxic disinfectants, and no ozone depletion or significant global warming occurred.

It is contemplated in an alternate embodiment that the composition of the blends could range from approximately 50 to approximately 91 percent by gas volume of CO₂, from approximately 9 to approximately 26 percent by gas volume of EtO, and from approximately 0.1 to approximately 24 percent by gas volume of CF₃I.

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The preceding examples can be repeated with similar success by substituting the generically or specifically described reactants and/or operating conditions of this invention for those utilized in the preceding examples.

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Although the invention has been described in detail with particular reference to these preferred embodiments, other embodiments can achieve the same results. Variations and modifications of the present invention will be obvious to those skilled in the art and it is intended to cover in the appended claims all such modifications and equivalents.

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The foregoing description comprises illustrative embodiments of the present invention. Having thus described exemplary embodiments of the present invention, it should be noted by those skilled in the art that the within disclosures
5 are exemplary only, and that various other alternatives, adaptations, and modifications may be made within the scope of the present invention. Merely listing the steps of the method in a certain order does not constitute any limitation on the order of the steps of the method. Many modifications and
10 other embodiments of the invention will come to mind to one skilled in the art to which this invention pertains having the benefit of the teachings presented in the foregoing descriptions. Therefore, it is to be understood that the invention is not to be limited to the specific embodiments
15 disclosed and that modifications and other embodiments are intended to be included within the scope of the appended claims. Although specific terms are employed herein, they are used in a generic and descriptive sense only and not for purposes of limitation. Accordingly, the present invention is
20 not limited to the specific embodiments illustrated herein, but is limited only by the following claims.